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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/597,347 | 07/21/2006 | Nobuo Ichihashi | SHG-050P2-319 / OSP-20263 | 9707 |
| 26875 7590 10/03/2008 WOOD, HERRON & EVANS, LLP 2700 CAREW TOWER 441 VINE STREET CINCINNATI, OH 45202 | | | EXAMINER HOBBS, LISA JOE | |
| | | | ART UNIT 1657 | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/597,347 | Applicant(s) ICHIHASHI ET AL. | |
| | Examiner Lisa J. Hobbs | Art Unit 1657 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 9-35 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 9-35 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/07, 12/06, 10/06, 8/06, 7/06</u> . | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Information Disclosure Statement

The information disclosure statement(s) (IDS) submitted on 21 July 2006, 15 August 2006, 19 October 2006, 12 December 2006, and 14 March 2007 is/are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Examiner Note

It appears that additional PCT paperwork was received by USPTO 05 June 2008 and 11 June 2008, wherein the claims, abstracts and specification are duplicates of the originals. The examiner has used the amended claim set dated 21 July 2006 for the examination since there is a Preliminary Amendment of the same date indicating that the amended claims, claims 9-35, are the active claim set.

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Claim Status

Claims 9-35 are active in the case. Claims 1-8 have been cancelled by preliminary amendment. Claims 9-35 are under examination; no claims are withdrawn as drawn to a non-elected invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 11, 13, 15-16, 18-20, 22-24, 26-30, 32-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Uchida et al. (US 5,516,675 A). Uchida et al. disclose a method wherein they: “[c]ontact milk and related raw material containing at least one of lactoperoxidase, secretory component, and lactoferrin to a [weak, carboxymethyl (col. 3, line 46)] cation exchanger. Selectively elute lactoperoxidase with an aqueous solution or a buffer having ionic strength of 0.2-0.5” (col. 2, lines 44-54), with “[t]he resultant lactoperoxidase, secretory component, and/or lactoferrin solutions are concentrated, desalted or dried, if necessary. The concentration is carried out by various methods such as evaporation under vacuum, ultra-filtration and reverse osmotic pressure filtration. The desalination is performed by conventional methods and techniques such as ultrafiltration, dialysis tube, electrodialysis, ion-exchanger resin and gel filtration. The drying is done by lyophilization, spray drying and so forth. ” (col. 6, lines 12-18), and that “lactoperoxidase with purity of 80% or over can be normally obtained” (col. 4,

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lines 63-65). They teach that “[a] fraction containing lactoperoxidase, secretory component, and lactoferrin can also be obtained by elution with an aqueous solution or a buffer having pH over 5 (five) and ionic strength over 0.5” (col. 4, lines 42-45). They teach that “[t]he aqueous solution and buffer used for the elution have no particular limit and include buffers of organic acids such as acetate, citrate and dimethylglutarate, and glycine buffer can be used. Sodium chloride may be added to increase the ionic strength” (col. 4, lines 57-63).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uchida et al. (US 5,596,082), Burling (US 5,149,647 A), Kussendrager et al. (US 6,010,698 A) and Souppe (FR 2841747, as evidenced by US 7,247,331 B2), and Lihme et al. (US 5,780,593). Uchida et al. teach “[l]actoperoxidase, secretory component and lactoferrin are separated in high purity from milk and related materials such as whey with a single cation exchange resin. After adsorption on the cation exchange resin, elution is carried out with an aqueous solution having an ionic strength and pH selected to elute each separately. Lactoperoxidase is eluted first, secretory component second and lactoferrin last. Each is obtained in a purity of about 80% or greater. The cation exchange resin can be a cross-linked polysaccharide, cellulose or an acrylamide resin having carboxyl, sulfonic acid or phosphoric acid functional groups which may be attached with a spacer” (abstract) and “[t]he eluted lactoperoxidase, secretory component, and lactoferrin solutions were concentrated separately using an ultrafiltration membrane having molecular weight cut-off of 50,000 down to 1.5 L volume, desalted to give electroconductivity of 0.2 mS/cm with an electrodialysis membrane and lyophilized to give 19.7 g of lactoperoxidase at purity of 85%” (Example 3).

Burling teaches that “[t]he microfiltered milk serum is then passed at a high rate (about 1-1.5 bed volumes per minute) through a column packed with a strong cation exchanger which selectively adsorbs lactoperoxidase and lactoferrin. The elution of the ion exchange mass is started by washing the milk serum out of the column with a buffer, preferably a phosphate buffer

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at the pH of the milk serum, 6.5. Subsequently, impurities, if any, are eluted with a buffer solution containing a weak saline solution, preferably of an inorganic alkali, alkaline earth or ammonium salt, for example 0.075 M NaCl. After this preparatory elution, the desired proteins are selectively eluted with buffer solutions containing saline solutions selected from the above-mentioned salts, at different concentrations. Thus, the elution of lactoperoxidase is performed at a salt concentration in the range of 0.10-0.4 M, and of lactoferrin at a salt concentration within 0.5-2 M. After this treatment, the proteins concerned have been concentrated about 500 times. The pure protein fractions are collected, and then a further concentration is preferably effected by ultrafiltration followed by desalination and freeze-drying so as to obtain a commercial product consisting of about 90% pure protein fractions” (col. 3, line 42 - col. 4, line 17 .

Kussendrager et al. teach “lactoferrin and lactoperoxidase can be eminently recovered from milk or milk products on an industrial scale [when] adsorbed to a cation exchanger by passing milk or a milk product at a high superficial velocity (more than 500 cm per hour) and at a high liquid load (100-600 bed volumes per hour) over the cation exchanger and then eluting the cation exchanger with a number of salt solutions of different concentrations. Thus a lactoferrin-containing fraction and a lactoperoxidase-containing fraction are obtained, which can be further treated in a conventional manner” (col. 1, lines 15-25) and that “[t]he cation exchanger to which the components from the milk or milk derivative are adsorbed can be any conventional cation exchanger in this field of the art” (col. 3, lines 23-25). They teach “elution with a solution of a low NaCl concentration, for instance of between 0.15 and 0.25 molar, yields a fraction containing substantially lactoperoxidase” (col. 4, lines 1-3). As well, Kussendrager et al. state that “[t]he fractions obtained, containing substantially lactoferrin and lactoperoxidase

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respectively, can be further treated according to conventional methods. These methods can comprise the steps of desalting, concentration, removing bacteria, and drying” (col. 4, lines 16-18). Also disclosed is that “the binding capacity of the ion exchanger is more than 10 g lactoperoxidase and more than 10 g lactoferrin per liter bed volume, and wherein more than 80% of the lactoperoxidase and lactoferrin is extracted” (claim 3).

Soupe teaches “a process for isolating milk proteins from milk or whey comprising the following steps: a) the milk or the whey is sterilized and defatted; b) the milk fraction derived from step a) is passed over a cation-exchange resin conditioned in an elution column; c) the fraction retained on the resin is eluted with an aqueous salt solution; d) the eluate resulting from step c) is desalted, preferably by ultrafiltration and diafiltration, and then sterilized, preferably by microfiltration” (US col. 2, lines 44-54). Soupe teaches the use of strong acid groups, but discloses that separation of milk proteins can comprise methods “such as electrodialysis or passage over weak anionic and cationic resins” (US col. 5, lines 22-23).

Lihme et al. teach “method[s] of isolating a biomolecule such as a protein or peptide from a medium containing biomolecules by ion exchange” (abstract) wherein the biomolecule can be lactoperoxidase (claim 4). They teach that “it was observed that ion exchangers of the weak type e.g. non-quarternary amine based anion exchangers such as diethylaminoethyl (DEAE)-based ion exchangers and carboxylic acid based cation exchangers can be eluted so that the neutralization of the ion exchanging (charged) groups on the ion exchange resin provide an uncharged resin. Further, it was observed that a gradual neutralization of the charged ion exchanging groups functioning as a buffer substance ensured that the bound and released biomolecule was kept in a medium having a low salt content and non-extreme pH-values which were acceptable to the

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eluted biomolecules. This gradual neutralization is against the general teaching of ion exchange chromatography... where anion exchangers are taught to be eluted with a decreasing pH gradient and cation exchangers are taught to be eluted with an increasing pH gradient. Further, this ensures that no buffer substances are required in the eluant, because the buffering effect is associated with the ion exchanging groups of the ion exchanger” (col. 4, lines 12-34).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Uchida et al., Burling et al., Kussendrager et al., Souppe, and Lihme et al. to achieve the invention as recited in the instant claims. There is much prior art disclosing the use of weak cation exchange columns of any desired capacity to adsorb lactoperoxidase and then eluting the enzyme with salt solutions of any desired ionic strength. Subsequent treatment of the lactoperoxidase to concentrate the protein fraction is also known in the art, including ultrafiltration, to achieve a pure, solid lactoperoxidase of 80% or more.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Hobbs whose telephone number is 571-272-3373. The examiner can normally be reached on Monday to Friday, 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lisa J. Hobbs/
Primary Examiner
Art Unit 1657

ljh